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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,744	01/25/2001	Albert Peng Sheng Tseng	13030	7077

7590 03/27/2003

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	**PAPER NUMBER**
1642	12

DATE MAILED: 03/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,744	TSENG ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7 & 9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed 1/6/2003 (paper no 11) is acknowledged and entered into the record.

Election/Restrictions

2. Applicant's election with traverse of SEQ ID No: 1 in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the sequences represent a single inventive entity, linked by a special technical feature, namely that they are phospholipase inhibitors. This is not found persuasive because the sequences represented by that of SEQ ID No: 1-33 represent both protein and nucleotide sequences which would prove to be a burdensome search to the examiner. There are many databases that are required in the search for both protein and or nucleotide sequences of which the search would exhaust the resources of the US Patent office. As such the sequence elected in the species election only constitutes a starting ground form which the searches are to be conducted.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-13 are pending, claims 9 is withdrawn from further consideration as being drawn to a non-elected invention. Therefore, claims 1-8 and 10-13 are examined on the record to the extent that it reads on SEQ ID No: 1.

Drawings

4. New corrected drawings are required in this application because figure 5/17 is labeled "figure 1", thereby making two figure ones present in the case. Applicant is advised to employ the services of a competent patent draftsperson outside the Office,

as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. **The requirement for corrected drawings will not be held in abeyance**.

Information Disclosure Statement

5. The Information Disclosure Statements filed 3-22-2002 & 7-26-2002 (paper nos. 7 & 9-) are acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Rejections - 35 USC § 112, 2nd paragraph

6. Claims 1-8, 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Regarding claims 1, 12, and dependent claims thereof in the recitation of the term "effective amounts", it is unclear from the specification as to what amounts are intended to be effective. The specification has not provided the skilled artisan with any dosages or requirements of any amount so that s/he would know that the amount added was indeed "effective".

8. Regarding claim 1, 11, 12, 13, and dependent claims thereof in the recitation of the term "derivative and homologues", it is unclear from the specification as to what these derivatives or homologues are intended to encompass. The specification has provided a broad definition as to what these terms are but has not provided one of skill in the art with the actual derivatives or homologues are to encompass.

9. Regarding claims 2, 5, and 10 in the recitation of the term "reduce", this is a relative term of which the specification has not provided a base level from which to measure the amount of reduction. As such the metes and bounds of the term cannot be established.

10. With regard to claims 1-8, and 10-13 in the recitation of the term "phospholipase inhibitor", it is unclear as to what this term is intended to encompass. Does the applicant intend to include ricin as an inhibitor of phospholipase.

11. With regard to claim 7 in the recitation of the term "derived", it is a relative term of which the specification has not defined. The derivation criterion has not been defined.

12. With regard to claims 8 and 9 in the recitation of the term "substantially", it is a relative term of which the specification has not defined. Substantially as it is interpretd in the claim can be as little as one and as much as 99% identity to the sequence set forth in the claims.

13. Regarding claims 11 and 13, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

14. Claims 1-8, and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how much, time of administration, dosage, and in what regimen.

Claim Rejections - 35 USC § 112, 1st paragraph

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1-8, 10-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case has only set forth a sequence consisting of SEQ ID No: 1and is not commensurate in scope to claims that read on derivatives, homologues, functional equivalents, or amino acid sequences that are 60% identical to that of SEQ ID No: 1.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

What are allelic variants? Reiger et al (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular

chromosome..... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined, nor in this case, is the structure of allelic variant proteins encoded by allelic variant genes defined. With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed structure of the encompassed proteins or encoded variants and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The amino acid sequence itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Although these court findings are drawn to DNA art, the findings are clearly applicable to the claimed proteins.

Furthermore, although drawn specifically drawn to the DNA art the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly applicable to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or

physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

No disclosure, beyond the mere mention of derivatives, homologues, functional equivalents, or proteins that are 60% identical to that of SEQ ID No: 1 is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only sequences having an amino acid sequence represented by that of SEQ ID No: 1 meets the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 112, 1st paragraph

17. Claims 1-8 and 10-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing the growth of a solid tumor or a method in the reduction of the cancer (adenocarcinoma or carcinoma) growth in cell expressing elevated levels of PLA2 comprising the administration of SEQ ID No: 1, does not reasonably provide enablement for a method of controlling the growth or development of any and all cancers with any and all types of phospholipase inhibitors so as to inhibit any and all cancers nor does it provide enablement for a biological composition that comprises any and all PLA2 inhibitors to be used as a prophylactic agent against cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or practice the invention commensurate in scope with these claims.

The claims of the instant invention are drawn to a method of controlling the growth or development of cancer comprising the administration of a phospholipase inhibitor. The claims are also drawn to a biological composition comprising inhibitors of phospholipase A_2 wherein the intended use of the composition is for the treatment and or prophylaxis of cancer in a subject.

The specification of the instant application teaches that the administration of a venom derived from a snake is a potent phospholipase A2 inhibitor and that the administration of the venom to a nude mouse model growing adenocarcinomas and carcinomas was able to inhibit and or reduce the volume of tumor injected into the mouse model. However, beyond that, the specification does not teach to one of skill in the art how to treat any and all forms of cancer using any and all types of phospholipase inhibitors. It is readily known in the art that cancer is an unpredictable and difficult disease to treat and inhibit. The specification has only provided the skilled artisan with the information to treat adenocarcinomas and carcinomas and no other. Because cancers have different etiologies and are known to have different treatment regimes, one of skill in the art would be forced to determine whether the administration of phospholipase inhibitors to other cancers would be able to combat cancer in the same manner. There is no teaching in the specification that would lead one of skill in the art to believe that the treatment of carcinomas and adenocarcinomas would be the same or similar to the treatment of leukemias or lymphomas. Furthermore, the specification contemplates the use of other forms of inhibitors, such as proteinaceous materials, lipids, polysaccharides, and other chemicals, theses are only desired embodiments of

which the specification does not specifically teach what they are or how they may or may not effect the methods of inhibiting or reducing of tumor burden. Other compounds such as lipids or chemical compounds may have more of a deleterious than efficacious effect on the treatment of cancer. There is no guidance in the specification to lead one of skill in the art to determine whether the use of other compounds other than venom derived from *N. scutatus* or *N. ater* are useful in the treatment of cancer. Further still, the specification is completely devoid of any disclosure that teaches compounds capable of being used as prophylatic vaccines for the treatment of cancers. There are no challenge studies present that would indicate that upon re-challenge of tumor to a subject administered with a prophylatic phospholipase inhibitor, that the subject would indeed be protected from developing the same tumor. In addition, there is no way for one of skill in the art to determine whom amongst the population would require the use of such an inhibitor because there are no known methods to determine who is predisposed to developing cancer. Therefore, given the broad recitation of the claims which read on any and all cancers, phospholipase inhibitors, and prophylatic compounds, one of skill in the art would be forced into undue experimentation to determine which cancers are treatable, which inhibitors are effective in treating cancer, and how and who to administer the prophylatic compounds so as to prevent the formation of cancer.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 1-8, and 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Wells A *et al* (WO 97/35588; 2 Oct 1997). Claims are drawn to a method of controlling the growth and development of a cancer comprising the administration to a subject a phospholipase inhibitor, wherein the subject is a human, wherein the inhibitor is able to reduce the cancer volume. Wells A *et al* disclose a method of treating cancer comprising the administration of a phospholipase inhibitor to a patient. Wells *et al* also disclose a composition comprising the phospholipase inhibitor in the presence of a pharmaceutical acceptable carrier. Since it is unclear as to what extent the term "substantially" is intended to encompass, the inhibitor disclosed by Wells A is substantially the same as that taught in SEQ ID No: 1.

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

21. Claims 1-8, and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Prendergast E *et al* (WO 98/10776; 19 March 1998). Claims are drawn to a method of controlling the growth and development of cancer in a subject comprising the

administration of a phospholipase inhibitor, wherein the subject is a mammal (human), wherein the inhibitor is able to reduce the volume of the cancer, and wherein the inhibitor is capable of inhibiting more than one type of PLA2. Prendergast *et al* disclose a method of treating neoplasmia in a subject, human, wherein the inhibitor is capable of reducing the volume of the tumor and is able to inhibit more than one type of PLA2. Prendergast *et al* also teach a pharmaceutical composition that comprises one or more venoms which are inhibitors of a phospholipase. Since it is unclear as to what extent the term "substantially" is intended to encompass, the inhibitor disclosed by Prendergast *et al* is substantially the same as that taught in SEQ ID No: 1.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Uni1 1642
March 24, 2003

ALI R. SALIMI
PRIMARY EXAMINER